

Poster

FROM VASCULAR DYSFUNCTION TO BRAIN VULNERABILITY: BEHAVIORAL AND MOLECULAR CHANGES IN CHRONIC HYPERTENSION

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Chronic hypertension is one of the major vascular risk factors for neurological disorders, particularly those associated with cognitive decline. We hypothesize that differences in vascular supply across anterior and posterior cerebral territories may contribute to the differential vulnerability of catecholaminergic circuits involved in cognition and reward-related processes. To explore this hypothesis, we investigated behavioral, catecholaminergic and neurovascular alterations in a mouse model of prolonged nitric oxide synthase inhibition. C57BL/6 mice received Nω-Nitro-L-arginine methyl ester hydrochloride (L-NAME 100 mg/kg/day) for 12 weeks, with longitudinal monitoring of arterial blood pressure followed by behavioral and molecular assessments. L--NAME-treated mice exhibited increased arterial pressure, accompanied by alterations in novelty-driven exploration, spatial responses to object displacement and reward-associated contextual preference, despite largely preserved motor coordination. This behavioral profile was accompanied by a reduced number of tyrosine hydroxylase-positive (TH+) neurons in the locus coeruleus and midbrain (substantia nigra pars compacta and ventral tegmental area) and reduced catecholaminergic fiber density in the dorsal hippocampus. In parallel, vascular analyses revealed reduced ZO-1 coverage of CD31+ vessels in the midbrain, suggesting region-specific alterations in endothelial junction organization. Together, these findings outline a pattern of behavioral, catecholaminergic, and endothelial alterations following chronic L-NAME exposure, consistent with a potential association between endothelial dysfunction and catecholaminergic circuit vulnerability. They provide a rationale for investigating whether differences in the organization of anterior and posterior cerebral territories contribute to the susceptibility of catecholaminergic circuits supporting cognition and adaptive behavior.